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β-strand mimicry: Exploring oligothienylpyridine foldamers

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Protein-protein interactions (PPIs) are involved in many cellular processes; consequently, the discovery of small molecules as modulators of PPIs has become a challenge in medicinal chemistry. Structural mimetics of protein secondary structures could maintain or restore biological functions and should possess biological activity. Actually, the most challenging classes of PPIs are those mediated by β-sheet, which are implicated in a number of diseases. Only a few β-strand mimics have been published to date. This study presents an evaluation of oligothienylpyridyl scaffolds in view of their ability for β-strand mimicry. We have observed that a coplanar arrangement in thienylpyridyl systems can be obtained in several different ways. The presence of a nitrogen and sulfur atom in the junction vicinity introduces a coplanar arrangement as well as the presence on the nitrogen atom in the non-*ortho*-substituted systems. The introduction of an *ortho* substituent in a system with a nitrogen atom in the junction vicinity perturbs the two rings somewhat, but the system can achieve the coplanar arrangement, because the energy barrier is very low. The same behavior was observed in a non-*ortho*-substituted biaryl with only a sulfur atom in the junction vicinity. The X-ray structures showed that the compounds have a tendency to adopt a nearly coplanar conformation and the positions of methyl substituents coincide well with those of i, i + 2nd or i, i + 4th β-strand side chains. Therefore, the thienylpyridine scaffold opens the way to produce coplanar compounds mimicking β-strand side-chain distributions.

Biography

Jana Sopkova-de Oliveira Santos has completed her PhD from the University Paris XI (Orsay) and University of Charles (Prague). Since 2012, she is a Professor of General Chemistry and Biophysics at the University of Caen Normandy. She has published more than 110 papers in reputed journals.

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